September 15, 2021

National Institutes of Health
Office of Research on Women's Health
6707 Democracy Boulevard, Suite 400
Bethesda, MD 20817

Dear Dr. Barr:

We are a group of clinician and social science researchers from the Center for Women's Health Research and Innovation (CWHRI) at the University of Pittsburgh and affiliated universities who conduct and translate research focused on sex- and gender-related health across the lifespan and sexual and reproductive health outcomes, with particular attention to socially marginalized populations and those with chronic medical illness. Our research is grounded in the principles of person-centeredness and decisional autonomy, with the goals of advancing gender and racial equity in health. With these goals at the fore, we submit the following recommendations in response to the NIH request for assistance in identifying gaps in research and clinical practice pertaining to women's health.

1) **Expanding research related to the development and validation of meaningful measures:** A narrow focus on biological or genetic mechanisms of adverse clinical outcomes and health disparities has failed to produce significant understanding of or actionable solutions to maternal health issues, including preterm birth and maternal mortality. Social and structural factors are increasingly recognized as critical contributors to health. However, research focused on understanding the role of social and structural determinants, and their interplay with biological mechanisms, is limited due to the dearth of metrics that capture salient constructs related to health and health equity including the manifestations of systemic and internalized racism; relevant elements of the socio-cultural environment; and more nuanced measures of socio-economic status, race and ethnicity constructs, and gender and sexual identity. Development of these measures offer standalone value but can also facilitate rigorous research on the physiological mechanisms linking these factors to health outcomes.

   There is also a need for more nuanced person-reported measures of healthcare experiences that capture both processes and outcomes that are most meaningful to people with regard to their reproductive health and health care. Moreover, as evidence of disrespectful obstetric care, particularly for people of color, continues to emerge, we need measures that can better capture how clinicians and systems constrain or facilitate people's reproductive autonomy and whether they are or are not providing person-centered, respectful care.

2) **Building a more robust data infrastructure to support the study of severe maternal morbidity and mortality:** Because of the need for large sample sizes to study the rare outcomes of severe maternal morbidity and mortality (SMMM), researchers currently rely on existing data sources, including hospital discharge data and healthcare administrative data. (The CDC's pregnancy mortality surveillance system is not available to extramural researchers). Although these data sources provide valuable insights on the health of people before and during pregnancy, they are limited in several important ways: 1) they often preclude studies beyond the perinatal period; 2) they do not measure factors occurring outside of the healthcare system; 3) they do not commonly link maternal and neonatal outcomes and data; 4) they lack longitudinal data on offspring; and 5) they lack person-reported outcomes.

   A longitudinal, national pregnancy outcomes surveillance system is necessary to better understand the causes and consequences of SMMM. The system must incorporate social and structural determinants of health (see point #1

above) in addition to clinical data of parent-child dyads and must be able to follow people before, during, and after pregnancy. Data collection must also be large enough to provide statistical power to enable the study of rare conditions as well as capture important population subgroups, including veterans, race and ethnicity, LGBTQIA+ (Lesbian, Gay, Bisexual, Transgender, Queer/Questioning, Intersex, Asexual/Aromantic) individuals, people with disabilities, and people with chronic diseases. One potential model of building such a data system would be to link administrative clinical and socioeconomic data (to reduce participant burden) with primary data collection of person-reported outcomes. Such data systems are successfully used elsewhere. For example, the UK Obstetric Surveillance System (UKOSS) allows for study-specific data abstraction from a national pool of population data on severe complications of pregnancy [1]. In the US context, the National Health and Aging Trends Study (NHATS) links administrative healthcare data to person-reported data among persons 65 and older; data can then be broadly used to better understand aging processes and health [2].

Inadvertent harms of privacy violations and bias are a real consideration for large-scale databases, particularly when analyzed using opaque machine learning methods [3]. To minimize potential risk and maximize potential benefit, at both the individual patient and population level, each step of the creation and curation of this surveillance system can and should incorporate explicit processes for protecting patient autonomy, privacy, and representation. There is a need for fair, transparent, and equitable procedures for determining which patient data is collected and shared (including verifying the accuracy of this data by the patient), the methods with which that data is analyzed, and the how those findings are implemented in a learning system.

3) **Developing and testing innovative interventions that address system, social and structural determinants of health:** There has been a longstanding focus in biomedical research on intervening on individual-level behaviors to impact health outcomes. As we increasingly incorporate an equity and justice lens into our work, we must attend to the broader systemic, social, and structural determinants of health and health disparities. We recommend increased funding for pragmatic service delivery interventions (both inside and outside of the formal healthcare system) and novel social or policy interventions that address upstream determinants of health across the life-course. Centering the perspectives of those whom the intervention seeks to help is fundamental to these efforts to avoid perpetuating inequities and injustices. This is best accomplished through formal procedures and policies for research that require meaningful engagement of patient advisors and/or community partners (see below).

Increased emphasis on implementation science would help ensure that these interventions have maximal impact. Examples of interventions related to the 3 areas specified by the NIH call for responses could include digital solutions that leverage a rapidly evolving climate to better reach underserved populations; interventions involving expanded workforce (community health workers, doulas, etc); novel approaches to improve cervical cancer screening and HPV vaccination outside of the healthcare system; and new approaches to eliminate disparities in health literacy among marginalized populations at elevated risk of adverse pregnancy outcomes. Implied in all these suggestions is the need for meaningful measures (point #1 above) and patient-centeredness (e.g., inclusive, low-cost, minimal burden) to ensure progress toward our desired outcomes.

In addition, we would like to call attention to that fact that NIH funding for research on contraception and abortion care and access is severely limited, even excluded. Access to these services is a critical component of health and wellbeing and particularly salient in the setting of rising rates of maternal mortality and chronic disease. With the rapid proliferation of state-level policies restricting delivery of basic reproductive health care, the number of

individuals with limited access to these critical services continues to grow. As chronic medical conditions (e.g., obesity, hypertension, diabetes, substance use disorders) become more prevalent across the US population, they are supplanting traditional causes of pregnancy-related complications and death, such as hemorrhage. Optimizing medical conditions prior to pregnancy may be one key to prevention, underscoring the importance of access to patient-centered and holistic family planning care, which includes assessment of pregnancy preferences as well as provision of pre-pregnancy, contraception, and abortion care services. People with chronic medical conditions need information about both how their disease (and any related medications) could impact the health of their pregnancy and how pregnancy might impact their disease state so that they can make informed decisions about family formation and pregnancy timing. For those who want to avoid or delay birthing, access to the full range of contraceptive methods and abortion services is essential, especially since unplanned pregnancies in the setting of chronic medical conditions can increase risks of poor maternal and infant outcomes by precluding disease and medication optimization before pregnancy. Novel strategies to increase delivery of these services in diverse clinical settings, including in primary and specialty care, are urgently needed.

To increase the portfolio of research on social and structural determinants of health with an eye towards achieving gender and racial equity as recommended above, there is a need to increase support for critical stakeholders in the process, including:

- Increasing the racial and gender diversity of principal investigators and study section members. Suggestions to help actualize this recommendation include:
    - Creating channels of accountability to protect investigators' time. We propose that the NIH creates a secure reporting process that allows investigators to account instances of institutional fraud. We also propose that the NIH have the ability to withhold indirects from an institution if consistent instances of fraud and mismanagement of investigator time occur.
    - Creating a new scorable criterion for extramural research project grants evaluating the institution's demonstrated commitment to justice, equity, diversity, and inclusion (e.g., proportion of underrepresented faculty in leadership roles, wage equity, proportion of underrepresented faculty members and trainees).
    - Providing higher reimbursement for peer review.

- Requiring patient engagement and/or community partnerships and stakeholder engagement/ participation in the research process. Suggestions include:
    - Adding meaningful patient engagement and/or community engagement as scorable criteria in the grant review process. By systematically requiring researchers to consider patient perspectives and/or build connections to community partners, NIH can increase the potential for its funded projects to have timely and relevant impact on communities.
    - Minimizing the adverse consequences of payment for participation in research. Specifically, the fear of losing Medicaid and disability benefits (because of research payment income) should not interfere with people's ability to take part in research.

- o Incorporating a system similar to *The Voice of the Patient* at the FDA, which systematically gathers perspectives of patients through community forums on their experiences and the available therapies to treat their condition, would promote citizen-focused science within the NIH [4].
  - o Incorporating patient, community, and stakeholder voices in the development of RFAs

- Creating new focused, interdisciplinary study sections for these areas, including family planning health services

Thank you for the consideration of these comments and recommendations. We are happy to partner with the NIH in any way that may be helpful related to research and clinical practice pertaining to women's health.

On behalf of CWHRI faculty,
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Citations
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[3]   Rudin C. Stop explaining black box machine learning models for high stakes decisions and use interpretable models instead. Nature Machine Intelligence. 2019 May;1(5):206-15.
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